REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

As noted in the Office Action Summary, claims 1-20 are currently pending. Claims 6, 7, and 17-19 stand withdrawn. Applicant thanks Examiner Seharaseyon for discussing the captioned application with Applicant's representative on March 11, 2004.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-5, 8-16, and 20 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite. Claim 1 stands rejected as purportedly vague in the recitation of the precise number and order of adding enhancing agents and organic solvents to induce the production of interferon. Applicant respectfully submits that the number and order of adding enhancing agents and organic solvents in claim 1 would be clear to the skilled artisan, based on what is provided in the specification as-filed.

With regard to the number and order of adding enhancing agents and organic solvents, Applicant again emphasizes that claim 1 recites an enhancing agent in claim element (ii) that is selected from element (a) (organic compounds); element (b) (organic solvents); and a combination of (a) (organic compounds) and (b) (organic solvents). Thus, both the organic compounds of element (ii)(a) and the organic solvents from element (ii)(b), or a combination thereof, may act as the enhancing agent according to the invention. For example, Applicant refers the Examiner to the following locations in the specification as-filed:

- page 5, line 31 to page 6 , line 3 (reciting the selection of enhancing agents and combinations of same);
- page 6, lines 5-8 (reciting the "... addition of the compound and/or an organic solvent...");
- page 6, lines 13-16 (reciting "... theophylline as well as a solvent such as dimethylsulfoxide...");
- page 7, lines 27-34 (reciting "... enhancing agents in the form of xanthine, pyrimidinol and pyrimidinone or derivatives of anyone thereof and/or various organic solvents..."; and "The enhancing agent can increase the interferon yield either alone or in a combination of an organic solvent and the mentioned compounds");
- page 15, lines 7-13 (reciting "... different organic solvents as well as different purines and pyrimidines...");
- Example 1 (pages 12-13) and Figure 1A show organic solvents as enhancing agents;
- Example 1 and Figure 1B show a combination of organic solvent and the compound 2-ABMP as enhancing agent;
- Example 2 (page 13) and Figure 2 show organic compounds as enhancing agents;
- Example 3 (pages 13-14) and Figure 3 show a combination of the organic solvent DMSO and the compound theophylline as enhancing agent;
- Example 4 (page 14) and Figure 4 show a combination of the organic solvent NMP and the compound theophylline as enhancing agent; and
- Example 5 (pages 14-15) shows a combination of the organic solvent DMSO and the compound 2-ABMP as enhancing agent.

Applicant notes that in the Examples described above, when the enhancing agent is a combination of a purine/pyrimidine compound and an organic solvent, both components of the combination were added simultaneously or one immediately after the other. However, Applicant submits that this is not the only order in which the components may be added, as is made clear by the specification. In light of these comments, Applicant requests that this rejection be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1-5 and 10-16 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Goren *et al.* in view of Zahorska *et al.*

Goren *et al.* purportedly disclose a process to produce interferon-α in human monocyte and lymphocytes and purportedly used human peripheral blood lymphocytes and monocytes to produce interferon-α by inducing them with Sendai virus. However, the Office Action notes that Goren *et al.* do not disclose the use of xanthine and its derivatives for the increased induction of the interferon. Zahorska *et al.* purportedly disclose the increased production of interferon in the presence of theophylline, a xanthine derivative. The Office Action states that it would have been obvious to the skilled artisan to enhance the interferon production following the induction with virus of human monocyte and lymphocytes. Applicant respectfully traverses.

The present invention is directed to a process for the production of α-interferon comprising inducing human leukocytes via a virus and treating the leukocytes with an enhancing agent. The enhancing agent may be selected from organic compounds, or organic solvents or a combination of organic compounds and organic solvents.

As set forth in M.P.E.P § 2142, in order to establish a prima facie case of obviousness, three criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art references must teach or suggest all the claim limitations.

In the present case, 1) the references fail to recite the elements of the claimed invention, 2) there is insufficient motivation to modify the cited references in the manner proposed in the Official Action, and 3) there is no reasonable expectation of success of achieving the claimed invention.

Goren *et al.* disclose production of α-interferon (IFN-α) from human monocytes and lymphocytes. These leukocytes were induced with Sendai virus or NDV. Goren *et al.* neither disclose nor even suggest the use of any enhancing agent, let alone disclose the use of an enhancing agent as recited in the presently claimed invention.

Zahorska *et al.* fail to remedy the deficiencies of the primary reference. Zahorska *et al.* purportedly disclose a xanthine derivative. However, Zahorska *et al.* discloses the use of Lpa cells, a mouse cell line, which is a subline of L_{929} cells (see page 44, column 1, lines 11-13). L_{929} cells are derived from mouse connective tissue fibroblasts. In support, Applicant submits herewith an information sheet regarding L_{929} cells, from DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmBH, providing the derivation of L_{929} cells. While there is no information in Zahorska *et al.* of what type of IFN is detected, the skilled artisan would know that fibroblasts produce IFN-β, which is irrelevant for the present invention. Applicant further notes that Zahorska *et al.* induced the mouse fibroblast cell line with a combination of DEAE dextran and Poly I:C, which is not a virus. In support, Applicant submits herewith a product information sheet for Poly I:C (polyinosine-polycytidylic acid), showing that it is a synthetic analog of double stranded RNA, known to induce interferons.

In light of these comments, Applicant submits that that not only do the combined references fail to recite each element of the claimed invention, the references further fail to provide a motivation for the skilled artisan to combine the references and/or to have an expectation of success. Zahorska *et al.* disclose a method for non-viral induced production of IFN-β from a mouse fibroblast cell line, while the presently claimed invention is directed to virally induced production of IFN-α from human leukocytes. Without hindsight, the skilled artisan would not have any reasonable expectation of success in combining the two references. Applicant respectfully requests that this rejection be withdrawn.

Claims 8, 9, and 20 are rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Goren *et al.* in view of Johnston (U.S. Patent No. 4, 780,413).

The secondary reference, Johnston, purportedly discloses the use of pyrrolidones and other cyclic amides for enhancing the production of IFN in cells induced with Sendai virus. The Office Action states that it would have been obvious to the skilled artisan to enhance the interferon production following the induction with virus of human monocyte and lymphocytes, as described by Johnston, because Johnston discloses that the addition of pyrrolidinones, a cyclic amide increase the production of interferon. Applicant respectfully traverses.

As above, Johnston fails to remedy the deficiencies of the primary reference and fails to provide a motivation to combine the two references. Johnston uses (transformed) human lymphoblastoid cell lines, since this references states that primary human white blood cells are unfit for the production of suitable amounts of IFN-α for clinical purposes (*see* column 1, lines 17-20). In contrast, the present invention is directed to production of IFN-α from human leukocytes. It is well known

in the art that there are many fundamental differences between cell lines and primary cells as production systems for IFN-α. For example, these differences are evident in the present specification as-filed. Specifically, this is made evident from the specification at page 4, lines 34 to page 5, line 16. Thus, the cited references, do not provide motivation or even guidance as to how to combine them, and so there is no reasonable expectation of success from such a combination.

In fact, Johnston teaches away from the presently claimed invention, stating that "... primary human white blood cells... cannot provide the abundant amounts of α-interferon required for clinical purposes" (see column 1, lines 17-20).

In light of the above remarks, Applicant requests that the rejections under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. **02-4800**.

Respectfully submitted,

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